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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,253	01/30/2006	Manuela Villa	17766 (PC27648A)	8815

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EXAMINER	
YOUNG, SHAWQUIA	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,253	VILLA ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-20,22,23,25,27 and 29* is/are pending in the application.

4a) Of the above claim(s) *1-12,18,19,22 and 29* is/are withdrawn from consideration.

5)☒ Claim(s) *13-15, 17, 20, 23 and 25* is/are allowed.

6)☒ Claim(s) *27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15, 17-20, 22, 23, 25, 27 and 29 are currently pending in the instant application. Applicants have cancelled claim 28 in an amendment filed on June 23, 2008.

I. *Response to Arguments*

Applicant's arguments, filed June 23, 2008 with respect to the rejection of claim 27 under 35 USC 112, first paragraph as failing to comply with the enablement requirement have been fully considered but are not persuasive. The amendment, filed June 23, 2008, has overcome the rejection of claim 28 under 35 USC 112, first paragraph as failing to comply with the enablement requirement and the objection of claims 13-15, 17, 20, 23, 27 and 28 as containing non-elected subject matter have been withdrawn.

Applicants have amended claim 27 to limit the cancer therapy to carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma. Applicants have provided pharmacological data supports that the claimed compounds are inhibitors of various types of protein kinases. However, Applicants have not provided adequate date showing that the claimed compounds are inhibitors of Aur 1 or Aur-2. According the data provided by Applicants, only 1 of the 5 compounds tested inhibits Aur 1 and only 1

of the 5 compounds tested inhibits Aur 2. This data shows that only two compounds out of the five tested has inhibitory activity at Aur 1 or Aur 2. It would require undue experimentation to discover which compounds inhibit Aur 1 and which compounds inhibit Aur 2. All of the references provided by Applicants relate to Aurora kinases and possible use of Aurora kinase inhibitors in cancer therapy. Applicants have not provided any adequate support showing that the instant compounds can treat all of the various types of cancers embraced by claim 27. Not only would one of ordinary skill of the art have to perform experimentation to find out which compounds inhibit Aur 1 or Aur 2, additional experimentation would be required to determine which of Aur 1 or Aur 2 inhibitors would treat which of the various types of cancer claimed in claim 27. Cancer is a very broad genus of diseases which can be very complex. Applicants have to provide adequate data and support in the art that shows that inhibitors of Aurora 1 or Aurora 2 can be used to treat the various of cancers claimed by Applicants in claim 27. The Examiner has maintained the rejection of claim 27 under 112, first paragraph as failing to comply with the enablement requirement.

II. *Rejection(s)*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is a product comprising a compound of formula (I) as defined in claim 13 or a pharmaceutical composition thereof as defined in claim 25, and one or more chemotherapeutic agents, as a combined preparation for simultaneous, separate or sequential use in anticancer therapy wherein the cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art

would recognize that in regards to therapeutic effects of cognitive disorders by inhibiting protein kinase would make a difference.

Furthermore, there is a vast range of causes for the problem and biochemical pathways that mediate the various diseases and disorders encompassed by the instant claim. There is no common mechanism by which all, or even most, cancers encompassed by the instant claim arise and one treatment cannot be used to treat all of the encompassed diseases.

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. Cancer is a disease characterized by a population of cells that grow and divide without respect to normal limits, invade and destroy adjacent tissues, and may spread to distant anatomic sites through a process called metastasis (URL:http://en.wikipedia.org/wiki/ Cancer>). Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast. Symptoms and treatment depend on the cancer type and how advanced it is ((<URL:http://www.nlm.nig.gov/medlineplus/print/> cancer.html>). It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Treatment may include surgery, radiation, chemotherapy, immunotherapy, monoclonal antibody

therapy, etc. Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols. Because "cancer" refers to a class of diseases, it is unlikely that there will ever be a single "cure or treatment for cancer".

The amount of direction present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. There are no working examples present for the treatment of cancer using the claimed compounds.

Test assays and procedure are provided in the specification at pages 29-35 for Inhibition assay of cdk2/Cyclin A activity, Inhibition assay of cdk2/Cyclin E activity, Inhibition assay of cdk1/Cyclin B1 activity, Inhibition assay of cdk5/p25 activity, Inhibition assay of cdk4/Cyclin D1 activity, Inhibition assay of MAPK activity, Inhibition assay of PKA activity, Inhibition assay of EGFR activity, Inhibition assay of IGF1-R activity, Inhibition assay of Aurora-2 activity and Inhibition assay of Cdc7/dbf4 activity.

Applicants have provided data that shows that 1 out of the 5 compounds tested has inhibitory activity at Aurora 1 and that a separate compound out of the 5 compounds tested has inhibitory activity at Aurora 2. Receptor activity is generally unpredictable and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to a product comprising a compound of formula (I) as defined in claim 13 or a pharmaceutical composition thereof as defined in claim 25, and one or more chemotherapeutic agents, as a combined preparation for simultaneous, separate or sequential use in anticancer therapy wherein the cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral

nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma..

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which cancers would be benefited by the inhibition of protein kinase would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of the diseases.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The specification fails to provide sufficient support of the broad use of the claimed compounds of the invention in a product comprising a compound of formula (I) as defined in claim 13 or a pharmaceutical composition thereof as defined in claim 25, and one or more chemotherapeutic agents, as a combined preparation for simultaneous, separate or sequential use in anticancer therapy wherein the cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma

pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the claim.

III. *Conclusion*

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Kamal A Saeed, Ph.D./

Primary Examiner, Art Unit 1626